Background: Published data indicate that there is a significant treatment gap between the evidence for and the implementation of lipid-lowering therapy and that recidivism is as high as 60% at 1 year. The aim of this study is to examine the impact of a clinical pharmacy cardiac risk service (CPCRS) on lipid screening, control, and treatment outcomes.

Methods: A computer-generated list of all patients with documented coronary artery disease, enrolled in a CPCRS between March 1, 1998, and October 1, 2002, and followed up for a minimum of 6 months was obtained. Outcome measures were the percentage of patients with up-to-date lipid screening results and the percentage achieving low-density lipoprotein cholesterol (LDL-C) goals at enrollment in CPCRS and at study end.

Results: A total of 8014 patients (mean age, 69.3 years; 69.8% men) met the entry criteria. The mean duration of follow-up was 2.3 years. Most patients (97.3%) had up-to-date lipid screening results at study end compared with 66.9% of patients at baseline. At study end, a total of 72.9% of patients achieved a LDL-C level of less than 100 mg/dL (<2.6 mmol/L) compared with 25.5% at baseline. The mean ± SD LDL-C level for the cohort at study end was 89±24 mg/dL (2.3±0.6 mmol/L). Of patients receiving medication, most (84.8%) were receiving therapy with statins alone, whereas 11.7% were receiving combination therapy.

Conclusions: A CPCRS working in conjunction with a patient-tracking system can achieve improved lipid results in a large and inclusive cohort of patients with coronary artery disease. Our approach is unique in that the results were sustainable and demonstrate reduced recidivism.

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Despite longstanding efficacy data for managing dyslipidemias, a significant gap remains between widely accepted, evidence-based treatment guidelines and routine clinical practice. Fewer than 32% of patients hospitalized with acute myocardial infarction receive lipid-lowering therapy at the time of discharge. Overall, only 37% of patients with documented coronary artery disease (CAD) attain target low-density lipoprotein cholesterol (LDL-C) levels less than 100 mg/dL (<2.6 mmol/L). Even when prescribed appropriate therapy, patients with CAD discontinue lipid-lowering medications at rates as high as 60% during the first year. The physician- and patient-related issues can explain some of these observations; however, system and process barriers also likely account for the so-called treatment gap. In an effort to close the gap in cardiovascular prevention and improve outcomes in patients with CAD, the American Heart Association recently launched its “Get With the Guidelines” (GWTG) initiative, which focuses on hospital team strategies and tools to identify and ensure appropriate medical management for patients hospitalized with CAD. While this and other programs are having some impact, barriers remain. As a hospital-based initiative, there are few specific provisions to extend evidence-based strategies to the large number of individuals whose CAD-related hospitalization pre-dates GWTG. There is no assurance that gains achieved with GWTG will be maintained over time, especially as GWTG participants are discharged to the care of variably resourced and motivated outpatient practices and systems.

The Clinical Pharmacy Cardiac Risk Service (CPCRS) of Kaiser Permanente Colorado Region (KPCR), a group model health maintenance organization providing comprehensive medical care to more than 385,000 members in the Denver/Boulder area, has endeavored to address...
The database is used for ongoing clinical management, patient tracking, and quality improvement activities. Working in concert with each patients’ primary care physician, CPCRS staff contact patients regularly to review treatment regimens and medication adherence and to make any necessary treatment plan adjustments.

DATA COLLECTION

In April 2003, regional and CPCRS databases were used to identify all active KPCR patients with unequivocal CAD who had been enrolled in the service for at least 6 months. Data were collected through April 1, 2003. Patients were excluded if they were not actively monitored by CPCRS staff. To describe the lipid outcomes of patients enrolled in the service with regard to screening, initiation of lipid-lowering therapy, and achievement of LDL-C goals, patients who met the aforementioned entry criteria, regardless of the presence of lipid values, were included in the cohort.

Data collected at the end of the study included patient demographic information, the duration of enrollment in CPCRS, and cardiovascular risk factor status. Relevant laboratory and pharmacy data were also collected for all individuals in the cohort. Cardiovascular risk factors included age (≥45 years for men and ≥55 years for women), current smoking (≥1 cigarettes per day), hypertension (>140 mm Hg systolic or >90 mm Hg diastolic on at least 2 separate occasions or receiving antihypertensive medications), and positive family history (confirmed CAD prior to ages 33 years and 65 years for first-degree male and female relatives, respectively).

OUTCOME MEASURES

Primary outcome measures were the percentage of patients with up-to-date lipid testing results and those achieving goal LDL-C levels at study end compared with preenrollment status. Baseline values were used to determine up-to-date screening and lipid profile results (fasting or nonfasting) if performed within 12 months of CPCRS enrollment. Follow-up values were used if performed within 12 months of study end. Lipid goals were defined as recommended by the National Cholesterol Education Program Adult Treatment Panel III guidelines as follows: LDL-C goal of less than 100 mg/dL (<2.6 mmol/L), triglyceride goal of less than 150 mg/dL (<1.7 mmol/L), non–high-density lipoprotein cholesterol (non-HDL-C) goal of less than 130 mg/dL (<3.4 mmol/L), and HDL-C goal of 40 mg/dL or higher (≥1.0 mmol/L). Patients without baseline and follow-up lipid levels within 12 months of enrollment and study end, respectively, were included in the analysis; however, they were assumed to be “not screened” or “not at goal” to provide the most conservative estimate.

Secondary outcomes measured were the mean cohort preenrollment and study end total cholesterol, HDL-C, triglyceride, and non–HDL-C values, all lipid-lowering medications used at study end, and the specific type and dose of statin therapy (in simvastatin-equivalent doses), when used. A “simvastatin-equivalent” schema was used for ease of data presentation. For patients using statins other than simvastatin, statin doses at study end were converted to equivalent doses of simvastatin using the following equivalence ratios: 40 mg of simvastatin = 80 mg of lovastatin = 80 mg of pravastatin = 20 mg of atorvastatin. Finally, as a measure of medication adherence and overall recidivism, the number and percentage of patients who purchased prescribed lipid therapy within 3 months of study end were determined. Three months was chosen in light of KPCR policy that provides a maximum 2-month supply of prescription medication at 1 time.
STATISTICAL ANALYSIS

Demographic data are displayed as mean ± SD, medians, or proportions, where appropriate. Paired t tests were used for the continuous data to compare differences in lipid parameters between the 2 periods (baseline and final). The McNemar test was used to evaluate differences in dichotomous outcomes. For cases in which the underlying distribution of data was not normally distributed, the Mann-Whitney rank sum test was used. Percentages were used to display the proportions of patients screened, those achieving lipid targets, and the lipid-lowering agents used. Two-tailed P values less than .05 were considered statistically significant.

RESULTS

Of 8472 patients identified with unequivocal CAD and followed for a minimum of 6 months, 8014 (94.6%) were enrolled in CPCRS and included in the formal study analyses. Of the 458 patients not included in the cohort, 372 (8.1%) were receiving care solely through their primary care physicians. Patient demographic and cardiovascular risk status data at study end are summarized in Table 1. The duration of CPCRS follow-up for the 8014 patients included in the cohort was 2.3 ± 1.2 years and ranged from 6 months to 5.1 years; 30.1% of patients were followed up for 3 or more years.

ACHIEVEMENT OF LIPOPROTEIN TARGETS

The number of patients with up-to-date lipid testing results and the percentage attaining Adult Treatment Panel III goals at study end was statistically and clinically significant compared with pre-CPCRS enrollment as depicted in Figure 1. Cholesterol screening in the 8014 patients increased by over 30% (66.9% to 97.3%; P < .001). Of the 2.7% of patients with no documented lipid screening at study end, all had been prompted to do so by CPCRS and/or physician staff by telephone and mail on at least 1 occasion. At study end, the number of patients reaching the LDL-C goal of less than 100 mg/dL (<2.6 mmol/L) increased nearly 3-fold (from 25.5% to 72.9%; P < .001); 92.1% attained an LDL-C level of less than 130 mg/dL (<3.4 mmol/L) by study end (P < .001). The overall LDL-C level decreased from 119 ± 35 mg/dL (3.1 ± 0.9 mmol/L) to 89 ± 24 mg/dL (2.3 ± 0.6 mmol/L) (P < .001). Subset analyses of lipid data revealed that significantly more men met the LDL-C goal compared with women (74.6% vs 68.7%; P < .001). Significantly more patients older than 75 years met the LDL-C goal compared with younger patients (75.6% vs 71.5%; P < .001). Among the 5838 patients achieving LDL-C goal of less than 100 mg/dL (<2.6 mmol/L), LDL-C was reduced to 79±14 mg/dL (2.0 ± 0.4 mmol/L). Secondary outcome measures are summarized in Table 2.

Table 1. Patient Demographics in 8014 Cohort Members at Study End

<table>
<thead>
<tr>
<th>Demographic</th>
<th>Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean ± SD (range), y</td>
<td>69.3 ± 10.2 (32-93)</td>
</tr>
<tr>
<td>Male sex</td>
<td>5591 (69.8)</td>
</tr>
<tr>
<td>Duration of follow-up, mean ± SD, y</td>
<td>2.3 ± 1.2</td>
</tr>
<tr>
<td>Cardiovascular event history†</td>
<td></td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>5423 (67.7)</td>
</tr>
<tr>
<td>Angioplasty alone</td>
<td>2907 (36.3)</td>
</tr>
<tr>
<td>Angioplasty + stent</td>
<td>2579 (32.2)</td>
</tr>
<tr>
<td>Coronary artery bypass graft surgery</td>
<td>3187 (39.8)</td>
</tr>
<tr>
<td>Unstable angina</td>
<td>1195 (14.9)</td>
</tr>
<tr>
<td>Cardiovascular risk factors†</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>7781 (97.1)</td>
</tr>
<tr>
<td>Positive family history</td>
<td>2767 (34.5)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>5407 (67.5)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>2463 (30.7)</td>
</tr>
<tr>
<td>Smoking (current)</td>
<td>1204 (15.0)</td>
</tr>
</tbody>
</table>

*Data are given as number (percentage) of patients unless otherwise specified.
†Not mutually exclusive.

Table 2. Mean Cohort Preenrollment and End Study Lipid Values

<table>
<thead>
<tr>
<th>Lipoprotein</th>
<th>Value, Mean ± SD, mg/dL</th>
<th>P &lt; .001</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cholesterol (n = 5327)†</td>
<td>195.9 ± 39.2</td>
<td>169.2 ± 30.9</td>
</tr>
<tr>
<td>Triglycerides (n = 5266)†</td>
<td>185.9 ± 148.7</td>
<td>167.8 ± 104.1</td>
</tr>
<tr>
<td>LDL-C (n = 5284)†</td>
<td>118.6 ± 34.7</td>
<td>89.2 ± 23.6</td>
</tr>
<tr>
<td>HDL-C (n = 5302)†</td>
<td>43.2 ± 12.8</td>
<td>46.9 ± 13.1</td>
</tr>
<tr>
<td>Non-HDL-C (n = 5313)†</td>
<td>154.0 ± 39.0</td>
<td>122.2 ± 29.6</td>
</tr>
</tbody>
</table>

Abbreviations: HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.
SI conversion factors: To convert cholesterol to millimoles per liter, multiply by 0.0259; to convert triglycerides to millimoles per liter, multiply by 0.0113.
†N does not equal 8014 because the data are limited to patients for whom both premeasurements and postmeasurements were available.


USE OF LIPID-LOWERING MEDICATIONS

Data regarding the percentage of patients prescribed lipid-lowering therapy at study end are shown in Figure 2. Of the 6920 receiving lipid-lowering medication, 5871 (84.8%) were receiving statin monotherapy. Combination regimens were used in 11.7% of all patients receiving lipid-lowering medications; 95% of these regimens included statins. The remaining 3.5% of patients were receiving nonstatin monotherapy.

CHARACTERISTICS OF PATIENTS NOT AT GOAL

Table 3 compares the characteristics of the patients who did and did not achieve their LDL-C goal. Of the 27.2% patients in CPCRS who did not attain their LDL-C goal, most were prescribed a medication; moreover, the mean statin dose was 47% greater in patients not at goal compared with those at goal (simvastatin-equivalent dose, 50.9 mg vs 34.6 mg; P<.001). Of the 6920 patients receiving lipid-lowering therapy, 6132 (88.6%) had purchased a lipid-lowering prescription within 3 months of the study end. This number includes some patients who had been prescribed medications for more than 3 years. Significantly fewer patients who were prescribed medications but not at goal had purchased their medication within the 3-month window compared with those at goal (92.2% vs 78.2%, respectively; P<.001).

COMMENT

Our before-after study demonstrates that a centralized, clinical pharmacy specialist–managed program can be highly successful in assisting patients achieve their lipid goals. Given that virtually all patients with CAD in KPCR are enrolled into CPCRS, there was no appropriate control group available for this study. Of more than 8000 patients with CAD, 97.3% were screened for dyslipidemia, 86.3% were receiving lipid-lowering medication, and 72.9% achieved the LDL-C goal of 100 mg/dL (<2.6 mmol/L) by study end. Patients were enrolled in the service for a mean±SD of 2.3±1.2 years, demonstrating that these results can be sustained over time.

Numerous studies indicate that patients, particularly those at greatest risk for CAD, are not achieving the lipoprotein targets recommended by national guidelines.5-7,14 One study of 4888 patients determined that only 18% of patients with CAD had achieved their LDL-C goal, compared with 37% of patients with 2 or more cardiac risk factors but without CAD and 68% of patients with less than 2 cardiac risk factors and without CAD.2 These data are consistent with other studies, which indicate that patients at the greatest cardiovascular risk are not achieving LDL-C goals.6,14,15

The reasons for the so-called treatment gap have largely been unexplored. Patient, physician, and system factors likely contribute to the gap. Studies suggest that 50% of patients stop taking their statin therapy after 1 year.9,10 Physician-related factors such as relying on laboratory reports to confirm the presence or absence of dyslipidemia without regard to the patient’s cardiac risk may result in some patients with seemingly “normal” cholesterol levels being missed.10 Initiating starting doses of lipid-lowering therapy without the necessary dosage titrations can result in patients remaining on suboptimal doses to achieve lipid goals.14 Finally, the health care system is illness rather than prevention driven. Patients typically fail to present unless they have a specific complaint. Given that patients do not typically feel ill from dyslipidemias, unless there is a system in place to identify these patients, they may go undetected.
An example of an innovative disease management program primarily aimed at improving the system, CPCRS incorporates close follow-up for all patients. Every patient enrolled remains in the service for as long as they are a KPCR member. At each contact, patients are questioned to ensure that they are taking the medication as prescribed, following a low-fat diet, and exercising regularly. This has helped ensure that patients remain on their prescribed therapy. The service uses a Web-based patient-tracking system that aids in scheduling patients for follow-up laboratory measures, sending patient reminder letters, and tracking clinical outcomes. The tracking system is essential in ensuring that patients are not lost to follow-up, another reason that patients in the general population may not be achieving LDL-C goals.14

As CPCRS has continued to expand, concerns from health care providers were whether the results obtained early on with small numbers of patients would be sustained over time as enrollment continued to increase. In 1999, we reported that of 1716 patients, 48% had achieved LDL-C goals.13 Four years later and with 8014 patients enrolled, the service has managed to maintain the gains and actually increase the proportion of patients achieving LDL-C goals. The proportion of patients who have achieved target LDL-C goals represents an unselected group of patients, since CPCRS attempts to enroll all patients within KPCR who have documented and validated CAD.

Despite our best efforts, 27% of patients still have not achieved the target LDL-C. We believe that this does not reflect on poor systems management. This may be related to the clinical status of the patient because most of these patients begin therapy with aggressive doses of lipid-lowering medication (average statin dose was higher in patients not at goal compared with those at goal) and are less adherent. We report that more older patients (/>75 years) achieved LDL-C goal compared with younger patients, which is inconsistent with previous reports.17

There are likely numerous reasons for the success of CPCRS. The service is unique to other risk reduction programs in that it uses clinical pharmacy specialists who are experts in the overall medication management of CAD. The specialists have extensive knowledge of cardiovascular risk factor management, are experts in drug therapy, and use evidence-based clinical judgment in the medical management of patients. The service is aggressive in prompt implementation of lipid-lowering therapy in any patient with an LDL-C above goal. For patients who do not achieve goal at follow-up, lipid-lowering medication is titrated to maximal doses and combination therapy is used if necessary.

Several other centers have established programs in an attempt to close the treatment gap.16-24 One study conducted a retrospective review of patients with CAD enrolled into a physician-directed, nurse-managed program to determine the proportion of patients with an LDL-C level of less than 100 mg/dL (<2.6 mmol/L).18 A subset of patients from 1 of 140 medical practices were evaluated in this study, since the patients from this particular center received care via a computerized system of follow-up and lipid clinic protocols. Although the number of patients from the medical center evaluated was not reported, 100% were receiving lipid-lowering therapy, 97% had an LDL-C value documented in the medical chart within the past year, and 71% had achieved the LDL-C goal. Another program used a telephone-based computerized system managed primarily by dietitians.19 At baseline, a total of 1699 patients with CAD were evaluated and 34% had an LDL-C level less than 100 mg/dL (<2.6 mmol/L). Three years later, 2827 patients had been evaluated, and 61% had achieved an LDL-C level of less than 100 mg/dL (<2.6 mmol/L).

The design of this study has limitations. Because the study was not a prospective, randomized trial with a control group, we cannot be certain the results reported are a direct result of the efforts of CPCRS. The magnitude of the changes observed may, in part, reflect secular trends in better lipid management and better awareness of the benefit of lipid-lowering therapy. The results of this study are derived from patients enrolled in a managed care organization, which uses a closed medical system. Whether similar results using a similar method of patient care and follow-up can be obtained in the general population remains to be determined; however, as previously described, studies have indicated that improved lipid control can be obtained using community pharmacists, dietitians, and nurses.18-24 This report highlights improvements in surrogate outcomes. We are currently evaluating whether the service has improved the clinical outcomes, such as decreased cardiac event and hospitalization rates. The economic feasibility of implementing such a service is also being evaluated.

The duration of patient follow-up in CPCRS has allowed for reliable comment on the overall recidivism of patients in our program. Our global, “all-comer,” long-term approach to CAD management together with KPCR’s sophisticated, integrated systems yields unique perspectives for those interested in effectively replicating clinical efficacy trials results in a practical, real-world setting.

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